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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/586,338	08/15/2006	Shinji Yokoyama	2006_1127A	2790

513 7590 12/16/2008
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EXAMINER

ZAREK, PAUL E

ART UNIT	PAPER NUMBER
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1617

MAIL DATE	DELIVERY MODE
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12/16/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/586,338	Applicant(s) YOKOYAMA ET AL.	
	Examiner Paul Zarek	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5 is/are pending in the application.
 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-5 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. ____. |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>07/14/2006</u> . | 6) <input type="checkbox"/> Other: ____. |

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DETAILED ACTION

Status of the Claims

1. Claims 1-5 are currently pending. This is the first Office Action on the merits of the claim(s).

Priority

2. Applicant's claim for the benefit of a prior-filed international application PCT/JP04/19717 (filed on 12/22/2004) under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. The effective filing date of the instant application is 12/22/2004.

3. Acknowledgment is made of applicant's claim to Japanese patent application 2004-007955 (filed on 01/15/2004) for foreign priority under 35 U.S.C. 119(a)-(d). The priority date of the instant application is 01/15/2004.

Claim Rejections - 35 USC § 112 (1st paragraph)

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 2-4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for therapeutic agents for low-HDL cholesterolemia or arteriosclerosis, does not reasonably provide enablement for prophylactic agents for cholesterolemia or arteriosclerosis. The specification does not enable any person skilled in the art to which it

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pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

6. *In re Wands*, 858 F.2d at 736-40, 8 USPQ2d at 1403-07, set forth eight factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is “undue.” (MPEP § 2164.01(a))

a. *The breadth of the claim:* Claims 2-4 are drawn to probucol spiroquinone, probucol diphenquinone, probucol bisphenol, or salts thereof, that possesses therapeutic or prophylactic faculties.

“Prevent,” “prevention,” and “prophylaxis” are potent terms implying that the method of prevention, or a prophylactic agent will necessarily prevent low-HDL cholesterolemia or arteriosclerosis from occurring following administration of the prophylactic agent in every subject that receives the agent;

b. *Nature of the invention:* The nature of the invention is a probucol derivative which can stabilize ABCA1. The probucol derivative can be used to treat low-HDL cholesterolemia or arteriosclerosis;

c. *The state of the prior art:* Probucol has been demonstrated to be therapeutic for atherosclerosis (a form of arteriosclerosis) (Tardif, et al., Current Opinions in Lipidology, 2003, “Conclusions”) and cholesterolemia (Matsuzawa et al., American Journal of Cardiology, 1988, abstract). The art is silent with respect to probucol or its derivative preventing either arteriosclerosis or cholesterolemia;

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- d. *Level of one of ordinary skill in the art:* An ordinarily skilled artisan would be physicians or scientists investigating cardiovascular disorders. The level of skill would be high;
- e. *Level of predictability in the art:* Probucol and its derivatives are known to be therapies for arteriosclerosis and cholesterolemia;
- f. *Amount of direction provided by the inventor:* Applicant describes the mechanism by which probucol affects the HDL cholesterol synthesis pathway in which the probucol derivatives stabilize ABCA1 to increase generation of blood HDL concentration, which slows the transport of LDL into the blood, thereby “prophylactically acts on arteriosclerosis.” (instant specification pg 15, lines 24-35);
- g. *Existence of working examples:* Examples 2-4 demonstrate that probucol derivatives can increase HDL production, *in vitro*, and *in vivo*. Applicant has not disclosed any examples of probucol derivatives treating or preventing arteriosclerosis or cholesterolemia; and,
- h. *Quantity or experimentation needed to make or use the invention based on the content of the disclosure:* Applicants have demonstrated that probucol derivatives induce HDL synthesis, *in vitro*, and *in vivo*. These results agree with the prior art at the time the invention was made. The prior art also demonstrates that probucol and its derivatives are effective therapies for arteriosclerosis and cholesterolemia. Thus, although the instant specification does not provide any direction regarding the use of probucol or its derivatives to treat arteriosclerosis and cholesterolemia, there is sufficient guidance in the art to guide a skilled artisan to use the invention as therapy. However, this is not the case

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with respect to prevention. The dearth of direction in the instant specification with respect to preventing arteriosclerosis and cholesterolemia is not compensated by the prior art. Indeed, Examiner found no instances in the prior art in which administration of the claimed compounds prevented arteriosclerosis or cholesterolemia in every patient receiving the drug. Undue experimentation would be required to use the invention as claimed. Therefore, the rejected claims are not considered to be enabled for a prophylactic agent by the instant specification.

Claim Rejections - 35 USC § 112 (2nd paragraph)

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 4 recites “anti-Alzheimer drugs” as a drug with which a probucol derivative can be combined. It is unclear what an anti-Alzheimer drug is. If the Applicants' intention is for the probucol derivative to be combined with an anti-Alzheimer's disease drug, then Applicants should amend the claim accordingly. Such an amendment would overcome this rejection. For art purposes, Examiner interprets “anti-Alzheimer drug” to mean “anti-Alzheimer’s disease drug.”

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Stocker (International Application WO 02/04031, provided in IDS).

11. Claims 1-3 and 5 are drawn to an agent selected from the group probucol spiroquinone, probucol diphenoquinone, probucol bisphenol, and salts thereof. Claim 4 is drawn to a drug comprising one of the above-mentioned probucol derivatives and at least one drug selected from the group of antidiabetes drugs, therapeutic drugs for complications of diabetes, antiobesity drugs, antihypertensive drugs, antihyperlipidemic drugs, diuretics, antithrombic drugs, and anti-Alzheimer drugs. Claims 2, 3, and 5 claim an intended use for the agent (low-HDL cholesterolemia, arteriosclerosis, or increasing blood level HDL, respectively). Disclosure of intended use in the preamble is not given patentable weight since the body of the claims fully and intrinsically set forth all of the limitations of the claimed invention (i.e. the probucol derivatives or salts thereof) (MPEP § 2111.02(II)).

12. Stocker discloses a probucol-derived bisphenol (pg 5, formula II). Since Stocker teaches the same compound as the claimed invention, it is assumed that the probucol bisphenol inherently stabilizes ABCA1. Stocker also discloses a pharmaceutical composition (i.e. a drug)

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comprising the probucol bisphenol, and a co-antioxidant, which is an obesity drug. Therefore, Stocker anticipates all the limitations of the rejected claims.

13. Claims 1-3 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by McLean, et al. (Lipids, 1994, provided in IDS).

14. Claims 1-3 and 5 are described above.

15. McLean, et al., teach probucol, probucol spiroquinone, probucol diphenquinone, and probucol bisphenol (Fig 1). Although McLean does not teach that these compounds are ABCA1 stabilizers, their ability to stabilize ABCA1 would be inherent. Therefore, McLean, et al., anticipate all the limitations of the rejected claims.

Conclusion

16. Claims 1-4 are rejected.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul Zarek whose telephone number is (571) 270-5754. The examiner can normally be reached on Monday-Thursday, 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

PEZ

/Rita J. Desai/
Primary Examiner, Art Unit 1625